Eur J Pediatr (2003) 162: 554–555
DOI 10.1007/s00431-003-1207-x

RESEARCH LETTER

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Melatonin for treatment of sleeping disorders in children with attention deficit/hyperactivity disorder: a preliminary open label study

Received: 21 May 2002 / Accepted: 25 February 2003 / Published online: 3 June 2003

A dose of 3 mg melatonine reduces the time of falling asleep significantly in attention deficit/hyperactivity disorder (ADHD) subjects on methylphenidate treatment. Insomnia occurs in up to 54% in children with ADHD when using methylphenidate [4, 5] these problems can worsen up to 64% [1, 3].

Melatonin, a hormone secreted by the pineal gland, plays a role in the regulation of the circadian rhythm. Melatonin levels are low during daylight and high during darkness [6]. Hypnotic effects have been demonstrated in a dosage of 1–5 mg and in high dosage no toxificity could be shown [2]. Data on the effects of melatonin in children are scarce, and mostly confined to children with mental disabilities or blindness [5].

The aim of this open label study was to investigate whether melatonin could be used as a safe drug to treat insomnia problems in children with ADHD on methylphenidate medication. During a period of 1 year, 120 children were diagnosed with ADHD. All were prescribed methylphenidate. The effect was evaluated by clinical interview and psychological test (before and after medication). The children did not use any other hypnotic medication. Informed consent was obtained from all parents and patients.

Of the 27 children with insomnia originally included, 24 completed the study. Two patients dropped out, one because of aggressiveness and another due to reported nightmares. One patient was excluded because of incorrect recording of the data. The results of the 24 subjects are shown in Fig. 1. Due to incomplete data recording, the results of the long-term effects are only available from 13 subjects. Immediately after the start of melatonin treatment, the subjects fell asleep significantly earlier than before, varying between 15 min to 240 min, with a median value of 135 min.

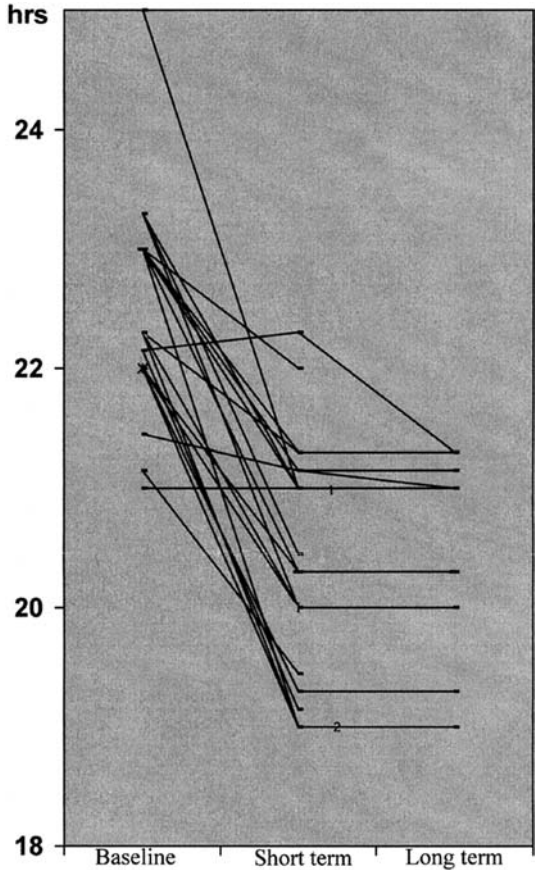

Fig. 1 Baseline recordings of falling asleep time in 24 subjects before melatonin medication. Short-term: recordings of falling asleep time after melatonin use (1–4 weeks) in 24 subjects. Long-term: recordings of falling asleep time after 3 months melatonin use in 13 subjects *Lines* 1 and 2 each represent the results of three properly registered long-term subject data

The long-term effect, after 3 months, was comparable with the immediate effect after 1 week. Also, a paired student *t*-test for the time of falling asleep before and

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after medication, proved to be significant ($t = 16.05$, $P < 0.01$). The time of falling asleep after melatonin had been given, varied between 15–64 min. Immediate relapse of insomnia was reported twice when treatment with melatonin had been forgotten during the study period and twice after ending the study. Restarted use of melatonin restored the positive effect.

Comparing the long-term effect to the immediate effect showed that melatonin remains for at least 3 months. No statistical difference could be shown in the short-term effect of melatonin between those patients who stopped recording data and those who did not ($P < 0.50$). Once a restless sleep was mentioned as a minor side-effect.

The data show that melatonin has a significant effect on the time of falling asleep. Although the study design, a placebo effect and the change of sleeping ritual could have influenced the results, the highly significant difference strongly suggests a positive melatonin effect. The one limitation was that since no laboratory set-up was available, the precise time of falling asleep could not be recorded exactly.

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